Remarks

Claims 32 and 34-44 and 46-55 are pending. Claims 48-50 are amended. Claims 51-55 are newly added. Claims 48-50 were amended to correct an error in the preamble of the claims.

Rejection Under 35 U.S.C. § 102

1. Claims 34, 39-44 and 47-48 were rejected under 35 U.S.C. § 102(e), as being anticipated by Lupski et al. (5,691,136). Applicants respectfully traverse this rejection.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

The passages of Lupski et al. cited in the Office Action fail to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. The passages of Lupski et al. cited in the Office Action also fail to disclose a kit for amplifying a target nucleic acid sequence, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, and wherein the set of primers has 3 or more primers.

Claims 34 and 39-44

Claim 34, as well as claim 39-44 that depend from Claim 34, are drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) a set of primers, wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, (see claim 34, lines 3-6) and (2) wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence (see claim 47, lines 6-8). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above.

The Office Action admits (page 4, lines 3-4) that Lupski et al does not explicitly disclose that each primer has a constant portion and a random portion. The Office Action however alleges (page 4, lines 13-15) that the teachings of Lupski et al. are inherent that each primer has a constant portion and a random portion and the constant portion of each primer are the same. For support, the Office Action cites Figure 3 of Lupski et al. that shows the alignment of ERIC oligonucleotide primer sequences with respect to the central inverted repeat of an ERIC consensus sequence.

In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden.

a. With regard to limitation (1) claim 34 is drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having

random nucleotide sequences, "wherein each primer comprises a constant portion and a random portion" (See claim 34, lines 3-6). In other words, each of the primers in the primer set must have both a constant and random portion.

Lupski et al. fails to disclose such a limitation. As described above, Lupski et al.discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). As provided in the Office Action, examples of the primers disclosed by Lupski et al. are specifically set forth in Figure 3. The Office Action alleges that the primers described in Figure 3 have a constant portion, TT, GGG, and AA and a random portion ATCG. Applicant first submits that the sequence "ATCG" is not present in any of the sequences shown in Figure 3. Secondly, Applicant's submit that each of the primers are specifically designed to hybridize to the ERIC consensus sequence. As such, the primers are all of a specific sequence and not of a random nature as required by the claims. In other words, the primers disclosed by Lupski et al. do not contain a random portion.

As such, the cited passage of Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 34 and 39-44.

b. With regard to limitation (2) claim 34 provides "wherein the constant portion of each primer has the same nucleotide sequence" (See claim 34, lines 6-8). In other words, each of the primers in the primer set must have both a constant and random portion and the constant portion of each primer in the set must be the same.

Lupski et al. fails to disclose such a limitation. The teachings of Lupski et al. are provided above. With respect to limitation 2, the Office Action again relies on Figure 3 of

Lupski et al. Applicant fist notes that the set of primers taught by Lupski et al. include primers that bind to opposite strands of the target sequences as shown in Figure 3. The primers of the primer set taught by Lupski et al include the ERIC1 and ERIC2 primers. Specifically, the primers of the primer set bind either the ERIC consensus sequence or the complement of the ERIC consensus sequence. For example, the ERIC1 primers bind to the ERIC consensus sequences whereas the ERIC2 primers bind to the complement of the ERIC consensus sequence. Applicants submit that it can easily be seen that the sequences of the ERIC1 and ERIC2 primers do not comprise any sequence that is the same for each primer. As such, Lupski et al. fails to disclose wherein the constant portion of each primer of a primer set has the same nucleotide sequence.

As such, the cited passage of Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 34 and 39-44.

Therefore, Applicants submit that Lupski et al. fails to disclose each and every element of the claims. Because Lupski et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Claims 47 and 48

Claim 47, as well as claim 48 that depends from Claim 47, are drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are

complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action alleges (page 4, lines 21-22) that the teachings of Lupski et al. anticipate the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Applicants first assert that the Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that disclose the above outlined limitation (1). Specifically, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, (1) wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Applicants submit that it would not be possible to point to such a description, as Lupski et al. fails to teach this element.

a. With regard to limitation (1) "wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target" there is no discussion, within the current Office Action. Nowhere, within the four corners of the current Office Action, is such a limitation addressed. In the interest of being thorough, Applicants wish to address the limitation, despite the Office Action's silence as to this limitation.

Claim 47 is drawn to a kit that comprises, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, line 3-5). In other words, each of the primers in the primer set hybridize to a different portion of the hybridization target.

Applicants first assert that the Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 102, the Patent Office is burdened with establishing that the cited art teaches each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that disclose the above outlined limitation (1). Specifically, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Applicants submit that it would not be possible to point to such a description, as Lupski et al. fails to teach these elements.

As described above, Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). As provided in the Office Action, examples of the primers disclosed by Lupski et al. are specifically set forth in Figure 3. The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence (see below for discussion on limitation (2)). However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above,

bind to the same portion of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are not complementary to a different portion of the hybridization target.

As such, the cited passage of Lupski et al. fails to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 47-48.

b. With regard to limitation (2) "wherein all of the primers in the set of primers are complementary to the same strand of the target sequence" Applicants first submit that "the same strand of the target sequence" does not include the complementary strand of the target sequence. This is supported at least on page 34, lines 25-31 of the application, where one of the amplification methods using a set of primers where all of the primers are complementary to the same strand of the target sequence is described. Specifically, it is provided that when a set of primers where all of the primers are complementary to the same strand of the target sequence are used, only one of the strands of the target sequence is replicated. This is due to the fact that the primers do not hybridize to the complementary strand. One of skill in the art would understand this to mean that the primers of the primer set only bind one of the strands, not both strands.

Lupski et al. fails to disclose such a limitation. As described above, Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). Applicant's first point out that there is an inconsistency in the Office Action as well as in the portions of Lupski et al. citred in the Office Action and the allegations in the Office Action. For example, the Office Action states on page 3, lines 23-25 that "each primer is selected to be substantially complementary to the *different strands* of each specific repetitive sequence to which the primer pairs bind" citing column 5, lines 15-22 of the instant specification (*Emphasis ours*). The Office Action admits that each primer in the primer pair or set binds to a different strand, this is not what is currently being claimed. Secondly, the portion of the Lupski et al cited in the Office Action (column 5, lines 15-

22) further provides the "each primer in the primer pair is selected to be substantially complementary to the *different strands* of each specific repetitive sequence" (*Emphasis ours).* Again this is not what is currently being claimed. What is being claimed is that each primer in the set of primers are complementary to the same strand of the target sequence. This is not disclosed in the portions of Lupski et al. cited by the Office Action. In fact, Lupski et al. teaches precisely the opposite, namely that the primers of the primer set bind different strands of the target sequence. In fact, the entire method disclosed by Lupski et al. require such a relationship between the primers of the primer set and the target sequence.

The Office Action later alleges (page 4, lines 7-9) that it is inherent within Lupski et al. that all of the primers in the set of primers are complementary to the same strand of the target sequence. The Office Action relies on Figure 3 of Lupski et al. for this allegation. Figure 3, much like column 5, lines 15-18 cited earlier, fails to teach such a limitation. As described above, Figure 3 shows the alignment of ERIC oligonucleotide primer sequences with respect to the central inverted repeat of an ERIC consensus sequence. Applicant fist notes that the set of primers taught by Lupski et al. include primers that bind to opposite strands of the target sequences as shown in Figure 3. The primers of the primer set taught by Lupski et al. include the ERIC1 and ERIC2 primers. Specifically, the primers of the primer set bind either the ERIC consensus sequence or the complement of the ERIC consensus sequence. For example, the ERIC1 primers bind to the ERIC consensus sequences whereas the ERIC2 primers bind to the complement of the ERIC consensus sequence. Applicants submit that it can easily be seen that the primers of Figure 3 are specifically designed to bind to different strands of the target (here the ERIC sequence) sequence. As such, Lupski et al. fails to disclose a kit wherein each primer in the set of primers are complementary to the same strand of the target sequence.

As such, the cited passages of Lupski et al. fail to disclose a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence. Because Lupski et al. fails to disclose every feature of the claimed kits, Lupski et al. fails to anticipate claims 47-48.

Therefore, Applicants submit that the Examiner has not met her burden of providing specific reference to where Lupski et al. discloses each and every element of the claims and furthermore, Lupski et al. fails to disclose each and every element of the claims. Because Lupski et al. fails to disclose every element of the claims, Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 103

1. Claims 32, 35-37 and 49 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

With regard to the subject matter of Claim 32, Applicants first note that Claims 35-37 and 49 all depend from Claim 32 and by definition encompass all the elements of Claim 32. Claim 32 is drawn to a kit for amplifying a target nucleic acid sequence, wherein the target sequence is double-stranded, having a first and a second strand, wherein the target sequence comprises an amplification target and a hybridization target, wherein the hybridization target comprises a right and left hybridization target, wherein the right hybridization target flanks the amplification target on one end and the left hybridization target flanks the amplification target on the other end, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein the set of primers comprises a right set of primers and a left set of primers, wherein the right set of primers has 4 or more primers and the left set of primers has 4 or more primers, wherein the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right

hybridization target, and wherein the complementary portions of the left set primers are (i) all complementary to the second strand of the target sequence and (ii) each complementary to a different portion of the left hybridization target.

As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 32, lines 8-9); (2) the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target (see claim 32, lines 11-14); and (3) (see claim 32, lines 14-16). It is important to note that each of in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

As discussed above, Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

The passages of Lupski et al. cited in the Office Action fail to disclose, fails to provide any teaching, motivation, or suggestion of a kit for amplifying a target nucleic acid sequence, wherein the target sequence is double-stranded, having a first and a second strand, wherein the target sequence comprises an amplification target and a hybridization target, wherein the hybridization target comprises a right and left hybridization target, wherein the right hybridization target flanks the amplification target on one end and the left hybridization target flanks the amplification target on the other end, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein the set of primers comprises a right set of primers and a left set of primers, wherein the right set of primers has 4 or more primers and the left set of primers has 4 or more primers, wherein the complementary

portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target, and wherein the complementary portions of the left set primers are (i) all complementary to the second strand of the target sequence and (ii) each complementary to a different portion of the left hybridization target. Furthermore, Lupski et al. teaches away from such a kit comprising the components claimed in Claim 32.

The Office Action alleges (page 5, lines 17-18) that the teachings of Lupski et al. make obvious the limitations of the claims. For support, the Office Action cites sections of Lupski et al. that describe methods of identifying strains of bacteria by genomic fingerprinting as well as specific sections directed to primers that can be used in the disclosed method. Applicants first assert that the Office Action fails to specifically address each and every limitation of the claims. In making a rejection under 35 U.S.C. § 103, the Patent Office is, in part, burdened with establishing that the cited art teaches or suggests each and every limitation of the claims. Applicants submit that the present rejection does not meet this burden. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that discloses or suggests wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Applicants submit that it would not be possible to point to such a description, as Lupski et al. fails to teach or suggest this element. Furthermore, Applicant submits that Lupski et al. in fact teaches away from such an element.

Since the Office Action fails to address the limitation "wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target", Applicant can merely attempt to understand where the Office Action may allege such a teaching or suggestion. As above, the Office Action relies on Lupski et al. for the same teachings as described above in the 35 U.S.C. § 102 rejection above. As described above, Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected

to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). As provided in the Office Action, examples of the primers disclosed by Lupski et al. are specifically set forth in Figure 3. The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence. However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are not complementary to a different portion of the hybridization target.

As such, the cited passage of Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence, wherein the target sequence is double-stranded, having a first and a second strand, wherein the target sequence comprises an amplification target and a hybridization target, wherein the hybridization target comprises a right and left hybridization target, wherein the right hybridization target flanks the amplification target on one end and the left hybridization target flanks the amplification target on the other end, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein the set of primers comprises a right set of primers and a left set of primers, wherein the right set of primers has 4 or more primers and the left set of primers has 4 or more primers, wherein the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target, and wherein the complementary portions of the left set primers are (i) all complementary to the second strand of the target sequence and (ii) each complementary to a different portion of the left hybridization target.

In fact, Lupski et al. actually teaches away from such a relationship between the primers of a primer set and the target sequence. Figures 2 and 3 of Lupski et al. illustrates the teaching

away, where each of the primers of the REP1 and REP2 or the ERIC1 and ERIC2 primer sets, respectively, bind to the same portion of the target sequence. For example, each of the ERIC1 primers in Figure 3 bind to the same portion of the ERIC consensus sequence while the ERIC2 primers in Figure 3 bind to the same portion of the complement of the ERIC consensus sequence. Nowhere in Lupski et al. is any other orientation of primers taught or suggested. The Office Action's reliance on Figure 3 for teaching or suggesting such a limitation is therefore incorrect.

The Office Action alleges (page 6, lines 21-23) that Lupinski et al. indicates that one of skill in the art will readily recognize the number and type of primers will depend on the kit as well as the sequences to be detected, however, the Office Action fails to provide any basis as to where one of skill in the art would not only chose the number of primers for a kit, but precisely the relationship of the primers to the target as required by the claims. Applicant submits such a teaching, motivation, or suggestion is not present and one of skill in the art, even armed with Lupski et al. would not be motivated to create such specific primers, but would actually be taught away from such a relationship as discussed above.

As such, Applicants submit that Lupski et al. fails to disclose or suggest each and every element of the claims. Accordingly, Lupski et al. fails to make obvious claims 32, 35-37 and 49. Applicants respectfully request withdrawal of this rejection.

2. Claims 38, 46 and 50 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Lupski et al. (5,691,136) as applied to claims 32, 34-37, 39-44 and 47-49 further in view of Blanco et al. (Journal of Biological Chemistry, 1989, Vol.264(15), pg. 8935-40). Applicants respectfully traverse this rejection.

In order for a reference or a combination of references to anticipate a claim or claims, "[f]irst, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." MPEP § 2143.

Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method

described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17).

Claim 38 that depends from Claim 32, Claim 46 that depends from Claim 34, and Claim 50 that depends from Claim 47, all refer to the polymerase of the respective kits. Specifically, each of the claims are drawn to Φ29 DNA polymerase. Aside from the specific enumeration of a DNA polymerase, Claims 38, 46, and 50 comprise all the limitations of the claims from which they depend.

Claim 38

With regard to the subject matter of Claim 38, Applicants first note that Claim 38 depends from Claim 32 and by definition encompass all the elements of Claim 32. As provided above, Claim 32 is drawn to a kit for amplifying a target nucleic acid sequence, wherein the target sequence is double-stranded, having a first and a second strand, wherein the target sequence comprises an amplification target and a hybridization target, wherein the hybridization target comprises a right and left hybridization target, wherein the right hybridization target flanks the amplification target on one end and the left hybridization target flanks the amplification target on the other end, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein the set of primers comprises a right set of primers and a left set of primers, wherein the right set of primers has 4 or more primers and the left set of primers has 4 or more primers, wherein the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target, and wherein the complementary portions of the left set primers are (i) all complementary to the second strand of the target sequence and (ii) each complementary to a different portion of the left hybridization target.

As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 32, lines 8-9); (2) the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target (see claim 32, lines 11-14); and (3) (see claim 32, lines 14-16). It is important to note that each of in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §103(a) rejection of claims 32, 35-37 and 49. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activty (See Office Action page 7, lines 9-10).

Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al. As discussed above in connection with the rejection under 35 U.S.C. § 103(a), the Examiner has not met her burden of establishing that Lupski et al. discloses or suggests a kit for amplifying a target nucleic acid sequence, wherein the target sequence is double-stranded, having a first and a second strand, wherein the target sequence comprises an amplification target and a hybridization target, wherein the hybridization target comprises a right and left hybridization target, wherein the right hybridization target flanks the amplification target on one end and the left hybridization target flanks the amplification target on the other end, the kit comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein the set of primers comprises a right set of primers and a left set of primers, wherein the right set of primers has 4 or more primers and the left set of primers has 4 or more primers, wherein the complementary portions of the right set primers are (i) all complementary to the first strand of the target sequence and (ii) each complementary to a different portion of the right hybridization target, and wherein

the complementary portions of the left set primers are (i) all complementary to the second strand of the target sequence and (ii) each complementary to a different portion of the left hybridization target. Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 38. Accordingly, Lupski et al. and Blanco et al.do not make obvious claim 38. Applicants respectfully request withdrawal of this rejection.

Claim 46

With regard to the subject matter of Claim 46, Applicants first note that Claim 46 depends from Claim 34 and by definition encompass all the elements of Claim 34. As provided above, Claim 34 is drawn to a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising a set of primers wherein the set of primers comprises primers having random nucleotide sequences, and a strand displacing DNA polymerase or a DNA polymerase and strand displacement factor compatible with the DNA polymerase, wherein each primer comprises a constant portion and a random portion, wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) a set of primers, wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion, (see claim 34, lines 3-6) and (2) wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence (see claim 47, lines 6-8). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 34, and 39-44. The Office Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activty (See Office Action page 7, lines 9-10).

Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al. As discussed above in

connection with the rejection under 35 U.S.C. § 102(e), Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence wherein the target sequence is a nucleic acid sample of substantial complexity, the kit comprising, in part, a set of primers wherein the set of primers comprises primers having random nucleotide sequences, wherein each primer comprises a constant portion and a random portion **AND** fails to disclose or suggest a the same kit wherein the constant portion of each primer has the same nucleotide sequence and the random portion of each primer has a random nucleotide sequence.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 46. Accordingly, Lupski et al. and Blanco et al.do not make obvious claim 46. Applicants respectfully request withdrawal of this rejection.

Claim 50

With regard to the subject matter of Claim 50, Applicants first note that Claim 50 depends from Claim 47 and by definition encompass all the elements of Claim 47. As provided above, Claim 47 is drawn to a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target, wherein all of the primers in the set of primers are complementary to the same strand of the target sequence, wherein the set of primers has 3 or more primers. As such, the claims require the set of primers to have specific attributes and abilities. In particular, the claims require: (1) that the each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target (see claim 47, lines 2-4) and (2) that all of the primers in the set of primers are complementary to the same strand of the target sequence (see claim 47, lines 4-5). It is important to note that each of the primers in the primer set of the kit must contain all the attributes listed above as well as the ability to interact with the hybridization target also described above.

The Office Action relies on Lupski et al. in the same way and for the same disclosure for which Lupski et al. was applied in the 35 U.S.C. §102(e) rejection of claims 47-48. The Office

Action further admits that Lupski et al. fails to specifically disclose a kit containing phage vphi 29 DNA polymerase for strand displacement activty (See Office Action page 7, lines 9-10).

As discussed above in connection with the rejection under 35 U.S.C. § 102(e), the Office Action fails to specifically address each and every limitation of the claims. In particular, the Examiner has failed to address or direct the Applicants attention to portions of Lupski et al. that disclose a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Applicants submit that it would not be possible to point to such a description, as Lupski et al. fails to teach these elements.

As described above, Lupski et al. discloses oligonucleotide primers and methods for identifying strains of bacteria by genomic fingerprinting (See Lupiski et al. column 1, lines 10-20). The method described by Lupski et al. employs primers that are used to amplify bacterial genomic DNA between repetitive sequences present in the bacterial genomes. (Id.) Each primer pair disclosed within Lupski et al. is selected to be complementary to the different strands of each specific repetitive sequence (See Lupski et al. column 5, lines 15-17). As provided in the Office Action, examples of the primers disclosed by Lupski et al. are specifically set forth in Figure 3. The primers described in Figure 3, as representative of the primers taught by Lupski et al. fall into two categories, those that bind the consensus/target sequence (sense) and those that bind the complement of the consensus/target sequence (antisense). Although the sense and antisense primers bind to different regions of the consensus/target sequence, they bind to different strands of the consensus/target sequence (see below for discussion on limitation (2)). However, each primer in the sense or antisense set, for example the ERIC1 and ERIC2 primers described above, bind to the same portion of the consensus/target sequence on the particular strand of the target sequence. In other words, each primer in the primer set are not complementary to a different portion of the hybridization target.

As such, Applicant further provides that Lupski et al. fails to disclose or suggest a kit for amplifying a target nucleic acid sequence, comprising, in part, a set of primers wherein the set of primers comprises a plurality of primers, wherein each primer comprises a complementary

portion, wherein the complementary portions of the primers are each complementary to a different portion of the hybridization target. Blanco et al. which was cited for disclosing that phage vphi 29 polymerase for strand displacement fails to supplement the elements missing from Lupski et al.

Thus, Lupski et al. and Blanco et al., either alone or in combination, fail to disclose or suggest each and every element of claim 50. Accordingly, Lupski et al. and Blanco et al.do not make obvious claim 50. Applicants respectfully request withdrawal of this rejection.

No fee is believed to be due with this submission; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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